

## PATENT COOPERATION TREATY

10/04/8134  
PCTNOTIFICATION OF THE RECORDING  
OF A CHANGE(PCT Rule 92bis.1 and  
Administrative Instructions, Section 422)

Date of mailing (day/month/year)
04 February 2002 (04.02.02)

Applicant's or agent's file reference
4-31102A

International application No.
PCT/EP00/07488

From the INTERNATIONAL BUREAU

To:

BECKER, Konrad  
Novartis AG  
Corporate Intellectual Property  
Patent & Trademark Property  
CH-4002 Basel  
SUISSE

## IMPORTANT NOTIFICATION

International filing date (day/month/year)
02 August 2000 (02.08.00)

## 1. The following indications appeared on record concerning:

the applicant     the inventor     the agent     the common representative

Name and Address WARTMANN, Markus Ruechligweg 75 CH-4125 Riehen Switzerland	State of Nationality CH	State of Residence CH
	Telephone No.	
	Facsimile No.	
	Teleprinter No.	

## 2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:

the person     the name     the address     the nationality     the residence

Name and Address WARTMANN, Markus Kornfeldstrasse 14 CH-4125 Riehen Switzerland	State of Nationality CH	State of Residence CH
	Telephone No.	
	Facsimile No.	
	Teleprinter No.	

## 3. Further observations, if necessary:

## 4. A copy of this notification has been sent to:

<input checked="" type="checkbox"/> the receiving Office	<input type="checkbox"/> the designated Offices concerned
<input type="checkbox"/> the International Searching Authority	<input checked="" type="checkbox"/> the elected Offices concerned
<input type="checkbox"/> the International Preliminary Examining Authority	<input type="checkbox"/> other:

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland  Facsimile No.: (41-22) 740.14.35	Authorized officer  Dorothée MÜLHAUSEN  Telephone No.: (41-22) 338.83.38
---	--

## PATENT COOPERATION TREATY

PCT

NOTIFICATION OF THE RECORDING  
OF A CHANGE(PCT Rule 92bis.1 and  
Administrative Instructions, Section 422)

Date of mailing (day/month/year) 28 September 2001 (28.09.01)	From the INTERNATIONAL BUREAU  To:  BECKER, Konrad Novartis AG Corporate Intellectual Property Patent & Trademark Property CH-4002 Basel SUISSE
Applicant's or agent's file reference 4-31102A	<b>IMPORTANT NOTIFICATION</b>
International application No. PCT/EP00/07488	International filing date (day/month/year) 02 August 2000 (02.08.00)

1. The following indications appeared on record concerning:	<input checked="" type="checkbox"/> the applicant	<input type="checkbox"/> the inventor	<input type="checkbox"/> the agent	<input type="checkbox"/> the common representative								
Name and Address NOVARTIS AG Schwarzwaldallee 215 CH-4058 Basel Switzerland	<table border="1"> <tr> <td>State of Nationality CH</td> <td>State of Residence CH</td> </tr> <tr> <td>Telephone No.</td> <td></td> </tr> <tr> <td>Facsimile No.</td> <td></td> </tr> <tr> <td>Teleprinter No.</td> <td></td> </tr> </table>				State of Nationality CH	State of Residence CH	Telephone No.		Facsimile No.		Teleprinter No.	
State of Nationality CH	State of Residence CH											
Telephone No.												
Facsimile No.												
Teleprinter No.												

2. The International Bureau hereby notifies the applicant that the following change has been recorded concerning:	<input type="checkbox"/> the person	<input type="checkbox"/> the name	<input checked="" type="checkbox"/> the address	<input type="checkbox"/> the nationality	<input type="checkbox"/> the residence							
Name and Address NOVARTIS AG Lichtstrasse 35 CH-4056 Basel Switzerland	<table border="1"> <tr> <td>State of Nationality CH</td> <td>State of Residence CH</td> </tr> <tr> <td>Telephone No.</td> <td></td> </tr> <tr> <td>Facsimile No.</td> <td></td> </tr> <tr> <td>Teleprinter No.</td> <td></td> </tr> </table>				State of Nationality CH	State of Residence CH	Telephone No.		Facsimile No.		Teleprinter No.	
State of Nationality CH	State of Residence CH											
Telephone No.												
Facsimile No.												
Teleprinter No.												

3. Further observations, if necessary:
--

4. A copy of this notification has been sent to:	<input checked="" type="checkbox"/> the receiving Office	<input type="checkbox"/> the designated Offices concerned
	<input type="checkbox"/> the International Searching Authority	<input checked="" type="checkbox"/> the elected Offices concerned
	<input checked="" type="checkbox"/> the International Preliminary Examining Authority	<input type="checkbox"/> other:

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland  Facsimile No.: (41-22) 740.14.35	Authorized officer  Elisabeth KÖNIG  Telephone No.: (41-22) 338.83.38
---	---

## PATENT COOPERATION TREATY

PCT

REC'D 31 OCT 2001

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 4-31102A	<b>FOR FURTHER ACTION</b>		See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/EP00/07488	International filing date (day/month/year) 02/08/2000	Priority date (day/month/year) 04/08/1999	
International Patent Classification (IPC) or national classification and IPC A61K9/127			
Applicant NOVARTIS AG et al.			

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 7 sheets, including this cover sheet.

This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

- I     Basis of the report
- II     Priority
- III     Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV     Lack of unity of invention
- V     Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI     Certain documents cited
- VII     Certain defects in the international application
- VIII     Certain observations on the international application

Date of submission of the demand 19/02/2001	Date of completion of this report 31.10.2001
Name and mailing address of the international preliminary examining authority:   European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer  Zimmer, B Telephone No. +49 89 2399 8600



# INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP00/07488

## I. Basis of the report

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):  
**Description, pages:**

1-12                   as originally filed

### Claims, No.:

1-7                   as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
  - the language of publication of the international application (under Rule 48.3(b)).
  - the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).
3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:
- contained in the international application in written form.
  - filed together with the international application in computer readable form.
  - furnished subsequently to this Authority in written form.
  - furnished subsequently to this Authority in computer readable form.
  - The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
  - The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.
4. The amendments have resulted in the cancellation of:
- the description,       pages:
  - the claims,           Nos.:
  - the drawings,       sheets:
5.  This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

# INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/EP00/07488

*(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)*

## 6. Additional observations, if necessary:

### III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:
  - the entire international application.
  - claims Nos. 7 regarding industrial applicability.

because:

- the said international application, or the said claims Nos. 7 regarding industrial applicability relate to the following subject matter which does not require an international preliminary examination (*specify*):  
**see separate sheet**
  - the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
  - the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
  - no international search report has been established for the said claims Nos. .
2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:
    - the written form has not been furnished or does not comply with the standard.
    - the computer readable form has not been furnished or does not comply with the standard.

### V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

#### 1. Statement

Novelty (N)	Yes:	Claims 1-7
	No:	Claims
Inventive step (IS)	Yes:	Claims
	No:	Claims 1-7
Industrial applicability (IA)	Yes:	Claims 1-6

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/EP00/07488

No: Claims

2. Citations and explanations  
**see separate sheet**

**VII. Certain defects in the international application**

The following defects in the form or contents of the international application have been noted:  
**see separate sheet**

**Re Item III**

**Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

Claim 7 relates to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of this claim (Art. 34(4)(a)(i) PCT).

**Re Item V**

**Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Reference is made to the following documents:

D1: WO 98 24427 A (ANGIOTECH PHARMACEUTICALS) 11 June 1998 (1998-06-11)

D2: LASIC D D: "Recent developments in medical application of liposomes: sterically stabilized liposomes in cancer therapy and gene delivery in vivo" JOURNAL OF CONTROLLED RELEASE, NL, ELSEVIER SCIENCE PUBLISHERS B.V. AMSTERDAM, vol. 48, no. 2-3, 13 October 1997 (1997-10-13), pages 203-222, XP004125857 ISSN: 0168-3659

The document D2 was not cited in the international search report.

2. Prior art document D1 discloses compositions comprising an anti-microtubule agent selected from a group of drugs comprising epothilone A or B as well as methods for treating or preventing inflammatory diseases like multiple sclerosis applying the anti-microtubule agent (claims 1 and 2). Furthermore, liposomes are disclosed as possible carriers to contain and deliver the therapeutic anti-microtubule agent (p. 32, l.26).

In view of the cited prior art the subject-matter of claims 1-7 of the present application seems to be new and thus fulfil the requirements of Art. 33(2) PCT.

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT - SEPARATE SHEET**

---

International application No. PCT/EP00/07488

3. Although the subject-matter of the present application seems to be new it does not involve an inventive step.

The problem of the present application seems to be the provision of a formulation for epothilone which decreases the unfavourable side effects while simultaneously improving the therapeutic efficacy of epothilone.

Prior art document D2 discloses several different modes of beneficial action of liposomes in drug delivery including the reduction of toxic side effects due to encapsulation of the toxic drugs (p. 204, right col., para. 3), biocompatibility and biodegradability (p. 203, left col., para. 1). Additionally, D2 discloses several formulations of conventional liposomes with encapsulated anticancer agents (p. 205, left col., last para.; Table 1).

In view of prior art document D2 the formulation of a liposomal composition comprising epothilone would be obvious for a person skilled in the art, especially as there is a hint in D1 that liposomes are suitable carriers for the anti-microtubule agent epothilone, which is administered to patients in need of it (see above item 2).

As a result, the subject-matter of claims 1 and 7 of the present application does not involve an inventive step (Art. 33(3) PCT).

Dependent claims 2-6 do not appear to contain any additional features which involve an inventive step when combined with the subject-matter of any claim to which they refer. Dependent claims are only allowable when related to a patentable independent claim (Rule 6.4 PCT).

4. For the assessment of the present claim 7 on the question whether it is industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT - SEPARATE SHEET**

---

International application No. PCT/EP00/07488

**R\_It\_m VII**

**Certain defects in the international application**

1. Contrary to the requirements of Rule 5.1(a)(ii) PCT, the relevant background art disclosed in documents D1 and D2 is not mentioned in the description, nor are these documents identified therein.
2. The units of measure employed on p. 5 of the description are not additionally expressed in terms of the units stipulated by Rule 10.1(a) PCT.
3. Due to the use of the expression "hereby incorporated by reference" (e.g. p. 1) the requirements of Rules 5 and 9.1 PCT are not met.

## PATENT COOPERATION TREATY

## PCT

## INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference <b>4-31102A</b>	<b>FOR FURTHER ACTION</b> see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. <b>PCT/EP 00/ 07488</b>	International filing date (day/month/year) <b>02/08/2000</b>	(Earliest) Priority Date (day/month/year) <b>04/08/1999</b>
Applicant <b>NOVARTIS AG et al.</b>		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 2 sheets.

It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
  - the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).
- b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :
  - contained in the international application in written form.
  - filed together with the international application in computer readable form.
  - furnished subsequently to this Authority in written form.
  - furnished subsequently to this Authority in computer readable form.
  - the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
  - the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2.  Certain claims were found unsearchable (See Box I).

3.  Unity of invention is lacking (see Box II).

4. With regard to the **title**,

- the text is approved as submitted by the applicant.
- the text has been established by this Authority to read as follows:

5. With regard to the **abstract**,

- the text is approved as submitted by the applicant.
- the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No.

- as suggested by the applicant.
- because the applicant failed to suggest a figure.
- because this figure better characterizes the invention.

None of the figures.

## INTERNATIONAL SEARCH REPORT

International Application No

PCT/00/07488

**A. CLASSIFICATION OF SUBJECT MATTER**  
 IPC 7 A61K9/127 A61K31/425

According to International Patent Classification (IPC) or to both national classification and IPC

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

WPI Data, PAJ, EPO-Internal, CHEM ABS Data

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 98 24427 A (ANGIOTECH PHARMACEUTICALS) 11 June 1998 (1998-06-11) claims 1,2 page 32, line 24 -page 33, line 19 -----	1,2,7



Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

## ° Special categories of cited documents :

- \*A\* document defining the general state of the art which is not considered to be of particular relevance
- \*E\* earlier document but published on or after the international filing date
- \*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- \*O\* document referring to an oral disclosure, use, exhibition or other means
- \*P\* document published prior to the international filing date but later than the priority date claimed

- \*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- \*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- \*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- \*&\* document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
14 December 2000	21/12/2000
Name and mailing address of the ISA  European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Authorized officer  Ventura Amat, A

**INTERNATIONAL SEARCH REPORT**

Information on patent family members

International Application No

PCT [REDACTED] 00/07488

Patent document cited in search report	Publication date	Patent family member(s)		Publication date
WO 9824427	A 11-06-1998	AU 5113298 A	BR 9713673 A	29-06-1998 31-10-2000

# INTERNATIONAL SEARCH REPORT

Ir. at Application No  
PCT/EP 00/07488

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61K9/127 A61K31/425

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

WPI Data, PAJ, EPO-Internal, CHEM ABS Data

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 98 24427 A (ANGIOTECH PHARMACEUTICALS) 11 June 1998 (1998-06-11) claims 1,2 page 32, line 24 -page 33, line 19 -----	1,2,7

Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

### \* Special categories of cited documents :

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier document but published on or after the international filing date
- "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- "O" document referring to an oral disclosure, use, exhibition or other means
- "P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search

Date of mailing of the international search report

14 December 2000

21/12/2000

Name and mailing address of the ISA  
European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
Fax: (+31-70) 340-3016

Authorized officer

Ventura Amat, A

**INTERNATIONAL SEARCH REPORT**

Information on patent family members

Inventor's name / Application No

PCT/EP 00/07488

Patent document cited in search report	Publication date	Patent family member(s)		Publication date
WO 9824427 A	11-06-1998	AU 5113298 A		29-06-1998